

Upon the Immunising Effects of the Intracellular Contents of the Typhoid Bacillus as obtained by the Disintegration of the Organism at the Temperature of Liquid Air." By ALLAN MACFADYEN, M.D. Communicated by LORD LISTER, O.M., F.R.S. Received February 19,—Read March 12, 1903.

In a previous communication\* it was shown that it was possible to disintegrate mechanically the typhoid bacillus at the temperature of liquid air, and to obtain the cell-juices of the organism.

The typhoid cell-juices obtained by this method on inoculation into animals proved toxic or fatal. It was, therefore, concluded that the typhoid bacillus contained within itself an intracellular toxin.

It remained to test the typhoid cell-juices for immunising and other properties. The preliminary experiments in this direction, which form the subject of the present note, were made upon the monkey. The monkey was selected as an animal most likely to furnish data of possible application to man. For this purpose the typhoid cell-juice was administered subcutaneously to the monkey. The injections did not produce any general symptoms beyond a transient rise in temperature, whilst the material was quickly absorbed after each injection without any traceable local effect. In this manner doses of 0.5 to 1 c.c. of the material were injected at intervals. An immediate result was the agglutination of the typhoid bacillus by the serum of the blood of the treated monkeys, whereas no such effect was produced by the serum of monkeys which had not been treated. This furnished useful evidence that the animals were under the influence of cell-juices derived from the typhoid organism. The injections were repeated at intervals of three to four days, and after a lapse of four to six weeks the animals were bled. The serum obtained was then tested for immunising properties. The test objects were (1) a virulent culture of the typhoid bacillus, and (2) the intracellular toxic juice of the same organism. A varying amount of the virulent bacilli and of their toxic cell-juice was mixed with a varying quantity of the serum. The respective mixtures were then injected into the peritoneal cavity of the guinea-pig.

The broth cultures of the typhoid organism used in the experiments were *per se* lethal in doses of 0.1 c.c. in five to ten hours. The typhoid cell-juices were fatal in doses of 0.2 and 0.1 c.c. in three to five hours, and in doses of 0.05 c.c. in about twelve hours. The serum was thus tested for (1) specific antibacterial and (2) specific antitoxic properties.

The experiments showed that the serum of the monkey, after injections of the typhoid cell-juices, possessed antibacterial and antitoxic properties, inasmuch as the serum protected the experimental animals

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against the bacilli, and also against an intracellular toxin obtained from them.

A simultaneous injection of (1) serum with the bacilli, and (2) serum with the toxic cell-juice produced no lethal or toxic effects. The control animals, on the other hand, invariably succumbed.

It was further investigated whether the serum possessed preventive and curative properties. The serum from treated monkeys was injected into guinea-pigs, one injection being made in each instance, and the same animals received at an interval of 12 to 24 hours lethal doses of the typhoid bacillus and of its toxic intracellular juice respectively. The treated animals survived the test, whilst the control animals succumbed. It was therefore concluded that the serum had protective properties.

A third series of guinea-pigs received lethal doses of the typhoid bacillus and of its toxic cell-juice respectively. The serum was then injected at various intervals into individual animals. It was found that the lives of the animals could be saved by one injection of the serum from a fatal infection or intoxication, even when half of the lethal period had elapsed in each instance. The serum, therefore, possessed curative properties.

In view of the above results it appeared desirable to test the effect of the typhoid cell-juices upon animals larger than the monkey, in order that a greater amount of serum might be obtained conveniently and tested quantitatively as regards antibacterial and antitoxic properties. These experiments are at present in progress, and the results will be communicated in due course.

From the experiments made upon the monkey it would appear:—

(1.) That by the injection of the intracellular juices of the typhoid organism into the monkey it is possible to obtain a serum with both antibacterial and antitoxic properties.

(2.) That such a serum possesses curative and preventive properties as regards the typhoid bacillus and an intracellular toxin present in the same organism.

It is believed that this research has afforded for the first time proof that, in the case of one species of pathogenic bacterium, the intracellular juices of the organism, when injected into a suitable animal, give rise to the production of a serum which is both bactericidal to the organism itself and antitoxic as regards a toxin contained in its substance. How far such properties of the cell-juice are shared by other pathogenic microbes must be the subject of further inquiry.

Experiments have been undertaken, with the aid of the cold-grinding methods referred to, with reference to other cells and organisms at the Jenner Institute of Preventive Medicine, where the above investigation has been conducted.